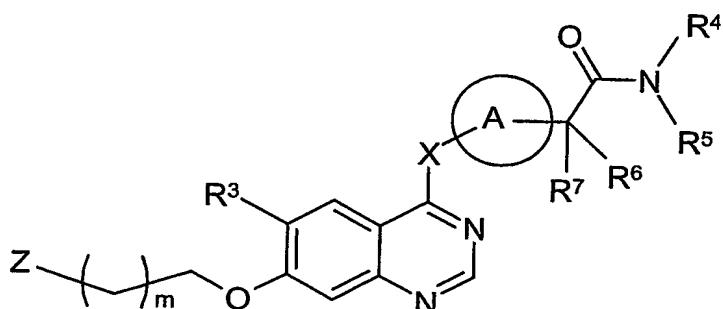


CLAIMS

1. A compound of formula (I):



formula (I)

5

wherein A is 5-membered heteroaryl containing a nitrogen atom and optionally containing one or two further nitrogen atoms;

X is O, S, S(O), S(O)₂ or NR¹⁴;

m is 0, 1, 2 or 3;

10 Z is a group selected from -NR¹R², phosphonooxy, C₃₋₆cycloalkyl which C₃₋₆cycloalkyl is substituted by phosphonooxy or C₁₋₄alkyl substituted by phosphonooxy, and a 4- to 7-membered ring linked via a carbon atom containing a nitrogen atom and optionally containing a further nitrogen atom, which ring may be saturated, partially saturated or unsaturated wherein the ring is substituted on carbon or nitrogen by phosphonooxy or C₁₋₄alkyl

15 substituted by phosphonooxy, and wherein the ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups;

R¹ is a group selected from -COR⁸, -CONR⁸R⁹ and C₁₋₆alkyl which C₁₋₆alkyl is substituted by phosphonooxy and optionally further substituted by 1 or 2 halo or methoxy groups;

R² is a group selected from hydrogen, -COR¹⁰, -CONR¹⁰R¹¹ and C₁₋₆alkyl which C₁₋₆alkyl is

20 optionally substituted by 1, 2 or 3 halo or C₁₋₄alkoxy groups or -S(O)_pR¹¹ (where p is 0, 1 or 2) or phosphonooxy, or R² is a group selected from C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

or R¹ and R² together with the nitrogen to which they are attached form a 4- to 7-membered ring optionally containing a further nitrogen atom which ring may be saturated, unsaturated or

25 partially saturated wherein the ring is substituted on carbon or nitrogen by a group selected from phosphonooxy and C₁₋₄alkyl which C₁₋₄alkyl is substituted by phosphonooxy or -NR⁸R⁹, and where the ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups;

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R³ is a group selected from hydrogen, halo, cyano, nitro, C₁₋₆alkoxy, C₁₋₆alkyl, -OR¹², -CHR¹²R¹³, -OC(O)R¹², -C(O)R¹², -NR¹²C(O)R¹³, -C(O)NR¹²R¹³, -NR¹²SO₂R¹³ and -NR¹²R¹³;

R⁴ is hydrogen or a group selected from C₁₋₄alkyl, heteroaryl, heteroarylC₁₋₄alkyl, aryl and 5 arylC₁₋₄alkyl which group is optionally substituted by 1, 2 or 3 substitutents selected from halo, methyl, ethyl, cyclopropyl and ethynyl;

R⁵ is selected from hydrogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl;

R⁶ and **R⁷** are independently selected from hydrogen, halo, C₁₋₄alkyl, C₃₋₆cycloalkyl, hydroxy 10 and C₁₋₄alkoxy;

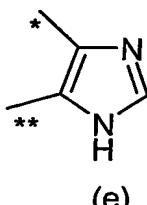
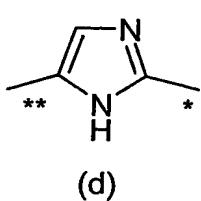
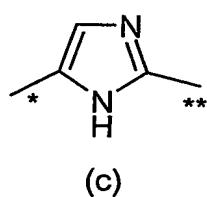
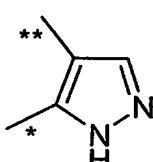
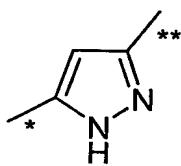
R⁸ is C₁₋₄alkyl substituted by phosphonoxy and optionally further substituted by 1 or 2 halo or methoxy groups;

R⁹ is selected from hydrogen and C₁₋₄alkyl;

R¹⁰ is selected from hydrogen and C₁₋₄alkyl (optionally substituted by halo, C₁₋₄alkoxy, S(O)_q, 15 (where q is 0, 1 or 2) or phosphonoxy);

R¹¹, R¹², R¹³ and R¹⁴ are independently selected from hydrogen, C₁₋₄alkyl and heterocyclyl; or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein A is a group of formula (a), (b), (c), (d) or 20 (e):



where * is the point of attachment to the X group of formula (I) and ** is the point of attachment to the (CR⁶R⁷) group of formula (I); or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 2 wherein A is a group of formula (a) as defined in claim 2; or a pharmaceutically acceptable salt thereof.

5 4. A compounds according to any one of claims 1, 2 or 3 wherein X is NH; or a pharmaceutically acceptable salt thereof.

5. A compound according to any one of the preceding claims wherein Z is $-NR^1R^2$ or a 5- to 6-membered saturated ring linked via a carbon atom containing a nitrogen atom and 10 optionally containing a further nitrogen atom, wherein the ring is substituted on carbon or nitrogen by phosphonoxy or C_{1-4} alkyl substituted by phosphonoxy; or a pharmaceutically acceptable salt thereof.

6. A compound according to any one of the preceding claims wherein R^1 is C_{1-5} alkyl 15 substituted by phosphonoxy and R^2 is a group selected from hydrogen and C_{1-6} alkyl which C_{1-6} alkyl is optionally substituted by 1, 2 or 3 halo or C_{1-4} alkoxy groups, or R^2 is a group selected from C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl and C_{3-6} cycloalkyl C_{1-4} alkyl; or a pharmaceutically acceptable salt thereof.

20 7. A compound according to any one of the preceding claims wherein R^1 is 2-phosphonoxyethyl; or a pharmaceutically acceptable salt thereof.

8. A compound according to any one of claims 1 to 5 where Z is $-NR^1R^2$ and R^1 and R^2 together with the nitrogen to which they are attached form a piperidine, pyrrolidine or 25 piperazine ring which is substituted by a group selected from phosphonoxy, phosphonooxymethyl, 2-phosphonoxyethyl, N -ethyl- N -(2-phosphonoxyethyl)aminomethyl and N -(2-phosphonoxyethyl)aminomethyl and where the ring is optionally further substituted by 1 or 2 methyl; or a pharmaceutically acceptable salt thereof.

30 9. A compound according to claim 8 wherein R^1 and R^2 together with the nitrogen to which they are attached form 2-(phosphonooxymethyl)pyrrolidinyl; or a pharmaceutically acceptable salt thereof.

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10. A compound according to any one of the preceding claims wherein R⁴ is 3-fluorophenyl, 3,5-difluorophenyl or 2,3-difluorophenyl; or a pharmaceutically acceptable salt thereof.

5 11. A compound according to any one of the preceding claims wherein R³ is C₁₋₄alkoxy, halo or hydrogen; or a pharmaceutically acceptable salt thereof.

12. A compound selected from:

- {1-[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]piperidin-4-yl}methyl dihydrogen phosphate;
- 10 2-[[3-(4-[(5-{2-[(3,5-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](ethyl)amino]ethyl dihydrogen phosphate;
- {(2S)-1-[3-(4-[(5-{2-[(3,5-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;
- 15 {(2R)-1-[3-(4-[(5-{2-[(3,5-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;
- {(2S)-1-[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;
- 20 2-[[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](propyl)amino]ethyl dihydrogen phosphate;
- 2-[[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](isobutyl)amino]ethyl dihydrogen phosphate;
- 25 2-[[3-(4-[(5-{2-[(3,5-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](isobutyl)amino]ethyl dihydrogen phosphate;
- 2-[(3-(4-[(5-{2-[(3,5-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](isobutyl)amino]ethyl dihydrogen phosphate;
- 30 2-[(2,2-dimethylpropyl)[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;
- 1-[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]piperidin-3-yl dihydrogen phosphate;

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{(2*R*)-1-[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;

2-[[3-(4-[(5-{2-[(3,5-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](prop-2-yn-1-yl)amino]ethyl dihydrogen phosphate;

5 2-[[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](isopropyl)amino]ethyl dihydrogen phosphate;

2-[[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](prop-2-yn-1-yl)amino]ethyl dihydrogen phosphate;

2-[[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-

10 methoxyquinazolin-7-yl}oxy)propyl](2-methoxyethyl)amino]ethyl dihydrogen phosphate;

2-{{[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl}amino}ethyl dihydrogen phosphate;

2-{{cyclobutylmethyl}[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

15 2-[[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl](3,3,3-trifluoropropyl)amino]ethyl dihydrogen phosphate;

2-{{allyl}[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

20 2-{{cyclobutyl}[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

2-{{cyclopentyl}[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

2-{{cyclopropyl}[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-

25 methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

2-{{cyclopropylmethyl}[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

2-{{cyclobutyl}[3-(4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-6-methoxyquinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

30 2-{{4-[(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]quinazolin-7-yl}oxy)methyl]piperidin-1-yl}ethyl dihydrogen phosphate;

2-[[3-(4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](ethyl)amino]ethyl dihydrogen phosphate;

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2-[[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](isopropyl)amino]ethyl dihydrogen phosphate;

3-{{3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]quinazolin-7-yl}oxy)propyl]amino}-3-methylbutyl dihydrogen phosphate;

5 2-{{(2*S*)-1-[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}ethyl dihydrogen phosphate;

{(2*R*)-1-[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;

2-[[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-10 quinazolin-7-yl}oxy)propyl](propyl)amino]ethyl dihydrogen phosphate;

2-[[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](butyl)amino]ethyl dihydrogen phosphate;

2-{{cyclopentyl[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

15 {(2*S*)-1-[3-({4-[(5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;

{(2*S*)-1-[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;

2-{{cyclopentyl[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-20 quinazolin-7-yl}oxy)propyl]amino}ethyl dihydrogen phosphate;

2-[[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](ethyl)amino]ethyl dihydrogen phosphate;

2-{{3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]quinazolin-7-yl}oxy)propyl]amino}-2-methylpropyl dihydrogen phosphate;

25 2-[[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](propyl)amino]ethyl dihydrogen phosphate;

{(2*R*)-1-[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl]pyrrolidin-2-yl}methyl dihydrogen phosphate;

3-[[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-30 quinazolin-7-yl}oxy)propyl](ethyl)amino]propyl dihydrogen phosphate

2-[[3-({4-[(5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1*H*-pyrazol-3-yl)amino]-quinazolin-7-yl}oxy)propyl](2-methoxyethyl)amino]ethyl dihydrogen phosphate

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2-[[4-(4-[{5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl]amino]-quinazolin-7-yl}oxy]butyl](propyl)amino]ethyl dihydrogen phosphate;

2-[[4-(4-[{5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl]amino]-quinazolin-7-yl}oxy]butyl](ethyl)amino]ethyl dihydrogen phosphate;

5 {*(2R)*-1-[4-(4-[{5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl]amino]-quinazolin-7-yl}oxy]butyl]pyrrolidin-2-yl} methyl dihydrogen phosphate;

2-[[4-(4-[{5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl}amino]quinazolin-7-yl}oxy]butyl](methyl)amino]ethyl dihydrogen phosphate;

{*(2S)*-1-[4-(4-[{5-{2-[(2,3-difluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl]amino]-10 quinazolin-7-yl}oxy]butyl]pyrrolidin-2-yl} methyl dihydrogen phosphate; and

2-{ethyl[3-({6-fluoro-4-[{5-{2-[(3-fluorophenyl)amino]-2-oxoethyl}-1H-pyrazol-3-yl}amino]quinazolin-7-yl}oxy)propyl]amino} ethyl dihydrogen phosphate; or a pharmaceutically acceptable salt thereof.

15 13. A pharmaceutical composition comprising a compound according to any one of the preceding claims in association with a pharmaceutically acceptable diluent or carrier.

14. Use of a compound according to any one of claims 1 to 12 in therapy.

20 15. Use of a compound according to any one of claims 1 to 12 in the preparation of a medicament for the treatment of a disease where the inhibition of one or more Aurora kinase is beneficial.

16. Use according to claim 15 wherein Aurora kinase is Aurora-A kinase or Aurora-B

25 kinase.

17. Use of a compound according to any one of claims 1 to 12 in the preparation of a medicament for the treatment of colorectal, breast, lung, prostate, pancreatic or bladder and renal cancer or leukemias or lymphomas

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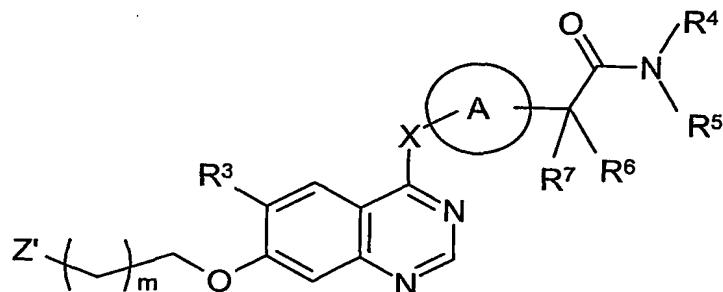
18. A method of treating a human suffering from a disease in which the inhibition of one or more Aurora kinases is beneficial, comprising the steps of administering to a person in need thereof a therapeutically effective amount of a compound as defined in claim 1 or a

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pharmaceutically acceptable salt thereof.

19. A method of treating a human suffering from colorectal, breast, lung, prostate, pancreatic or bladder and renal cancer or leukemias or lymphomas, comprising the steps of
 5 administering to a person in need thereof a therapeutically effective amount of a compound as defined in claim 1 or a pharmaceutically acceptable salt thereof.

20. A process for the preparation of a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt thereof, which process comprises converting a compound of
 10 formula (II) into a compound of formula (I) by phosphorylation of an appropriate hydroxy group:



formula (II)

where A, X, m, R³, R⁴, R⁵, R⁶, R⁷ and R⁹ are as defined for formula (I); and Z' is a group
 15 selected from -NR^{1'}R^{2'}, hydroxy, C₃₋₆cycloalkyl which C₃₋₆cycloalkyl is substituted by hydroxy or C₁₋₄alkyl substituted by hydroxy, and a 4- to 7-membered ring linked via a carbon atom containing a nitrogen atom and optionally containing a further nitrogen atom, which ring may be saturated, unsaturated or partially saturated wherein the ring is substituted on carbon or nitrogen by hydroxy or C₁₋₄alkyl substituted by hydroxy and wherein the ring is optionally
 20 further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups; R^{1'} is a group selected from -COR^{8'}, -CONR^{8'}R⁹ and C₁₋₆alkyl which C₁₋₆alkyl is substituted by hydroxy and optionally further substituted by 1 or 2 halo or methoxy groups; R^{2'} is a group selected from hydrogen, -COR¹⁰, -CONR¹⁰R¹¹ and C₁₋₆alkyl which C₁₋₆alkyl is optionally substituted by 1, 2 or 3 halo or C₁₋₄alkoxy groups or -S(O)_pR¹¹ (where p is 0, 1 or 2) or hydroxy, or R^{2'} is
 25 a group selected from C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₃₋₆cycloalkylC₁₋₄alkyl; or R^{1'} and R^{2'} together with the nitrogen to which they are attached form a 4- to 7- membered ring optionally containing a further nitrogen atom which may be saturated, unsaturated or

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partially saturated wherein the ring is substituted on carbon or nitrogen by a group selected from hydroxy and C₁₋₄alkyl which C₁₋₄alkyl is substituted by hydroxy or -NR⁸R⁹ and where the ring is optionally further substituted on carbon or nitrogen by 1, 2 or 3 halo or C₁₋₄alkyl groups; and where R⁸ is C₁₋₄alkyl substituted by hydroxy and optionally further substituted by 1 or 2 halo or methoxy groups:

and thereafter if necessary:

- i) converting a compound of formula (I) into another compound of formula (I); and/or
- ii) removing any protecting groups; and/or
- iii) forming a pharmaceutically acceptable salt thereof.